DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on **12/24/2009** has been entered.

Claims 33 and 78 have been canceled (Note- applicants incorrectly state cancellation of claim 79, on page 2, line 2 of the claim amendments, although intends to cancel claim 78, as presented on page 9 of the amendment).

Claim 79 has been newly presented.

Claims 1, 2, 4, 8, 12, 13, 15, 17, 20, 28, 29, 31, 34, 36, 39-41, 46, 49, 51, 61, 64, 66, 67, 69-77 and 79, as currently amended, are pending in this application.

Claims 1, 2, 4, 8, 12, 13, 15, 17, 20 and 28 remain withdrawn as non-elected invention.

Claims 29, 31, 34, 36, 39-41, 46, 49, 51, 61, 64, 66, 67, 69-77 and 79 (the elected invention of group III, as currently amended) are examined on their merits in this office action.

Claim Rejections - 35 USC § 112-Withdrawn

The rejection of claims 29, 31, 33, 34, 36, 39-41, 46, 49, 51, 61, 62, 64, 66, 67 and 69-78 under 35 U.S.C. 112, second paragraph as being indefinite, made in the previous office action, has been withdrawn in view of claim amendments submitted by applicants.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names **joint inventors**. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Claims 29, 31, 34, 36, 39-41, 46, 49, 51, 61, 64, 66, 67, 69-77 and 79 (as currently amended) are rejected under 35 U.S.C. 103(a) as being unpatentable over Chopra (WIPO document, WO 01/52822 A1; IDS) in view of Motoyama et al (US 4,751,241; 1988; previously cited by the examiner).

Claims (as currently amended) are directed to "a reduced coenzyme Q10-containing composition which **comprises** reduced coenzyme Q10, a polyglycerol fatty acid ester, and at least one member selected from the group consisting of a fat component, an oil component and a polyol,

wherein a content of the at least one member selected from the group consisting of a fat component, an oil component and a polyol is not lower than 50% by weight based on total weight of the composition minus a weight of coenzyme Q10; a content of the polyglycerol fatty

acid ester is **not higher than 40%** by weight based on total weight of the composition minus a weight of coenzyme Q10;

a content of Tween and/or Span species, **when** the same is further contained in the composition, is **not higher than 30%** by weight based on total weight of the composition minus a weight of coenzyme Q10; and wherein the fat component or oil component is at least one member selected from the group consisting of coconut oil, palm oil, palm kernel oil, linseed oil, camellia oil, brown rice germ oil, avocado oil, rapeseed oil, rice oil, peanut oil, corn oil, wheat germ oil, soybean oil, perilla oil, cottonseed oil, sunflower seed oil, kapok oil, evening primrose oil, shea butter, sal fat, cacao butter, sesame oil, safflower oil, olive oil, lard, milk fat, fish oil beef tallow, modified fat component, modified oil component, medium-chain fatty acid triglycerides, fatty acid partial glycerides, and phospholipids, wherein the modified fat component or modified oil component is derived from at least one member selected from the group consisting of coconut oil, palm oil, palm kernel oil, linseed oil, camellia oil, brown rice germ oil, avocado oil, rapeseed oil, rice oil, peanut oil, corn oil, wheat germ oil, soybean oil, perilla oil, cottonseed oil, sunflower seed oil, kapok oil, evening primrose oil, shea butter, sal fat, cacao butter, sesame oil, safflower oil, olive oil, lard, milk fat, fish oil, and beef tallow by a process selected from the group consisting of fractionation, hydrogenation and transesterification" (see instant claim 29, in particular).

Chopra (IDS) discloses a reduced coenzyme Q10-containing composition (see abstract, claims, and examples I-X, in particular) comprising reduced coenzyme Q10, a fat or oil, and a polyol (such as glycerol or other polyhydric alcohols). Chopra discloses reduced coenzyme Q10-containing compositions in various forms including oral dosage forms such as soft capsules, etc. which are "substantially ubiquinone-free" (i.e. the oxidized form of coenzyme Q10), and incorporate reducing agents, oils or fat, polyols, and one or more surfactants (see WIPO document, page 14, 5th paragraph, and examples I-X, in particular). Chopra discloses that such Co-Q10 (in an amount from 0.1% to 10% by weight; see Chopra, page 7, and ranges disclosed for examples III and IV, in particular) containing compositions may comprise components such as soybean oil, sunflower oil, safflower oil, rapeseed oil, fish oil, medium chain triglycerides, phospholipids (as recited in instant claim 62; see Chopra, page 12, last paragraph and various embodiments), surfactants (such as Tween 80, 20-90%; or Span 80, 1-15%; see examples I, III,

IV, VI, in particular), reducing agent such as vitamin C or ascorbyl palmitate (see Chopra, examples, and claim 2, in particular), **vitamin E acetate, D-alpha tocopherol, or esters thereof** (in an amount of 2-20%; see page 8, examples II, IV and X, in particular) and can be prepared or stored in a deoxygenated (such as prepared and sealed under nitrogen gas; see Chopra, page 21, example I, last paragraph, in particular).

However, a reduced coenzyme Q10-containing composition comprising **polyglycerol fatty acid ester** (as specifically recited in instant claims 70-72, such as **diglycerol monooleate**), and "wherein a content of the polyglycerol fatty acid ester is not higher than 40% by weight based on total weight of the composition minus a weight of coenzyme Q10" (as recited in instant claim 29), is not explicitly taught by the compositions disclosed by Chopra.

Motoyama et al (1988) discloses polyglycerol fatty acid esters (see abstract, summary of the invention, columns 1-2, in particular) such as diglycerol monooleate (see column 2, lines 23-30, in particular) to be used as emulsifying agents for drugs that are very slightly soluble in water (including ubiquinones, CoQ10; see column 2, lines 38-56, in particular; and also suitable for compositions comprising lipid-soluble reducing agents and/or nutrients such as vitamin E rich natural oils, shark liver oil, etc.) in order to enhance the absorption and thus bioavailability of said drugs (i.e. in a pharmaceutical composition) in the digestive tract when administered using oral dosage forms such as soft capsules (see columns 4-5, and examples), and wherein the content of polyglycerol fatty acid ester used in the composition for increasing the dispersibility of the drug is usually 0.05~30 parts by weight for one part by weight of the drug (see column 4, lines 53-56, and last paragraph; and examples, in particular).

Therefore, it would have been obvious to a person of ordinary skill in the pharmaceutical composition art to modify the reduced coenzyme Q10-containing composition of Chopra such that it contains (in addition to the surfactants such as Tween or Span) an emulsifying agent such as polyglycerol fatty acid ester as explicitly taught and exemplified by Motoyama et al.

One of ordinary skill in the art would have been motivated at the time of invention to make such modification in the composition taught by Chopra in order to obtain a better reduced coenzyme Q10-containing composition (having an enhanced absorption and bioavailability in the mammalian gut) as suggested by Motoyama et al, with a reasonable expectation of success.

The limitations, "wherein the content of the polyglycerol fatty acid ester is not higher than 40% by weight based on total weight of the composition minus a weight of coenzyme Q10" would have been obvious to a person of ordinary skill in the art at the time this invention was made as Motoyama et al disclose the suitability of a broad range of concentrations that can be used with a drug that is very slightly soluble in water (such as Co-Q10, and vitamin E containing drugs or nutrients) in order to improve its dispersibility and thus its bioavailability owing to the surface active properties of said polyglycerol fatty acid esters (see column 4, lines 38-42, in particular) when combined with the composition as claimed. The scope of the claimed subject matter, as currently presented by applicants, fails to patentably distinguish over the state of the art as represented by the cited prior art references of record.

With regard to the limitations (i.e. the content of the fat component or oil component or a polyol, on percent basis; claim 29, in particular), claim 36 (the content of ascorbic acid, on percent basis), claim 41 (the content of surfactant), claim 64 (the content of reduced CoQ10, on percent basis), and claim 67 (the content of polyglycerol fatty acid ester by weight, on percent

basis), it is to be noted that given the detailed disclosures of all the components and their amounts used for various preparations or dosage forms by Chopra and Motoyama et al (as discussed above), the adjustments to the amount and/or the contents and ratio of various components used in the composition would have been obvious to a person of ordinary skill in the pharmaceutical formulation art in order to achieve a better and stable composition containing reduced Coenzyme Q10. The claimed limitations of instant claims 46, 49, 51 and 69 are taken to be intrinsic to the composition taught by the cited prior art references of record, as discussed above.

As per MPEP 2144.06, "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

As per PPEP 2144.05 (R-3): In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. In re Wertheim, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); In re Woodruff, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990). Similarly, a prima facie case of obviousness exists where the claimed ranges and prior art ranges do not overlap but are close enough that one skilled in the art would have expected them to have the same properties. Titanium Metals Corp. of America v. Banner, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985). "[A] prior art reference that discloses a range encompassing a somewhat narrower claimed range is sufficient to establish a prima facie case of obviousness." In re Peterson, 315 F.3d 1325, 1330, 65 USPQ2d 1379, 1382-83 (Fed. Cir. 2003).

As per MPEP 2111.01, during examination, the claims must be interpreted as broadly as their terms reasonably allow. In re American Academy of Science Tech Center, F.3d, 2004 WL 1067528 (Fed. Cir. May 13, 2004)(The USPTO uses a different standard for construing claims than that used by district courts; during examination the USPTO must give claims their broadest reasonable interpretation.). This means that the words of the claim must be given their plain meaning unless applicant has provided a clear definition in the specification. In re Zletz, 893 F.2d 319, 321, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989).

Response to Applicant's Arguments

Applicant's arguments filed on 03/22/2010 (as they pertain to the pending claims of record) have been fully considered but they are not persuasive for the following reasons of record:

Applicants seem to arguing (see remarks, page 11, in particular) the unexpected benefits of using polyglycerol fatty acid ester in the claimed composition that enhances the stability of the reduced Co-Q10 containing composition without having adverse effect on the stabilization produced by the use of "fat and/or oil component and/or polyol", which is noted and fully considered. However, it is not found to be persuasive because all the components as recited in the claimed composition (i.e. the product as claimed) are explicitly taught and/or suggested and made obvious by Chopra when taken in combination with the disclosure of Motoyama et al (see also the obviousness rejection above), and therefore one would expect the same benefits in terms of stability and/or bioavailability, etc. Moreover, the composition as presented in claim 29 does not necessarily require a polyol (see Markush group for fat, oil, and polyol), or a polyglycerol fatty acid ester ("not higher than 40%.." taken as a range of 0-40% by weight, i.e. an optional component), or for that matter the surfactant "Tween and/or Span species" ("when the same is further contained…", i.e. optional component), which are needed in specific proportions to provide the unexpected benefits, as currently argued by applicants. In addition, instant claims do not require the limitations of degree of stability upon storage, etc., or the extent of enhancement in absorbability of the reduced Coenzyme Q10 in living body, etc., which are taken to be intrinsic to the composition disclosed in the cited prior art of record.

The argument that "*Motoyama describes the polyglycerol ester of an unsaturated fatty acid, but Motoyama does not disclose the preferable relationship between the content of the polyglycerol ester of an unsaturated fatty acid and the content of the fat component, the oil component and/or the polyol in the composition*", is not found to be persuasive because the prior art of Motoyama et al has been relied upon in the obviousness rejection of record to demonstrate the fact that, at the time the claimed invention was made, the use of emulsifiers such as diglycerol monooleate (i.e. a polyglycerol fatty acid ester) would have been obvious to a person of ordinary skill in the pharmaceutical art as they clearly suggest the fact that drug formulations comprising drugs that are very slightly soluble in water (including coenzyme Q10, also drug formulations such as vitamin E rich natural oil, etc.) can be stabilized by use of polyglycerol fatty acid esters, which enhance their dispersibility and overall bioavailability *in vivo* (see Motoyama et al, rejection above). Thus, the argument that "*Motoyama et al only describes coenzyme Q10 (ubidecarenone: oxidized coenzyme Q10) on column 2, lines 55-56, and does not describe reduced coenzyme Q10*", is noted. However, it is not found to be persuasive because Motoyama et al disclose compounds or drugs, which are known to be reducing agents and that are very slightly soluble in water (for example, vitamin E containing nutrients, etc.) that can be suitably stabilized using the polyglycerol fatty acid esters disclosed by them.

The argument (see remarks, page 13) that "*As shown in the Declaration under 37 CFR 1. 132 filed with the Response after Final Office Action, in the composition containing polyglycerol fatty acid and not higher than 30% by weight of Tween80 high stability of reduced coenzyme Q10 was achieved, but in the composition containing higher than 30% by weight of Tween80 the stability of reduced coenzyme Q10 was extremely inhibited. In addition, as shown in Examples*

23-24 in the present specification, the composition containing no Tween80 also shows high stability of reduced coenzyme Q10. However, Chopra and Motoyama neither disclose nor suggest such excellent effects of the present invention", is noted and fully considered. However, it is not found to be persuasive because the instant claim 29, as presented, does not necessarily require the presence of said surfactant "Tween80" (i.e. "***when*** the same is further contained in the composition, is not higher than 30%.."; taken as 0-30% range, which is optional), as currently being argued by applicants. It is noted that the compositions (and the specific amounts and/or proportions of components) that provided the specific results and unexpected benefits as argued by applicants (i.e. example 18-22 of the instant disclosure, and instant remarks) are not currently recited in the claimed invention. Since the scope of the claims is not commensurate with the showing presented in the form of a declaration from Takahiro Ueda, the composition as claimed remains rejected over the combined teachings of the cited prior art references of record under 35 USC 103(a).

Obviousness-type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference

claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

1. Claims 29, 31, 34, 36, 39-41, 46, 49, 51, 61, 64, 66, 67, 69-77 and 79 (as currently amended) **are** provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 16-19 of copending Application No. **11/586,511** (filed in US on 10/26/2006; common inventors; and same assignee, Kaneka Corporation, Japan). Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application also claims a reduced coenzyme Q10-containing composition (processed as an oral dosage form) comprising reduced coenzyme Q10, oil and fat, a polyglycerol fatty acid ester, along with a reducing agent, ascorbic acid. Since the two sets of

composition claims are co-extensive in their scope, an obviousness-type double patenting rejection is required.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to ODP Arguments

Applicant's arguments regarding the ODP rejection of record have been fully considered but they are not persuasive for the following reasons of record. Applicants argue the following (see remarks filed on 03/22/2010; page 13, last paragraph):

> "...Claim 29 recites the amounts of Tween and/or Span, which are not recited in claim 16 of SN 11/586,511. Accordingly, it is requested that this rejection be withdrawn. This rejection if need be will be further addressed once the other rejections have been overcome"

In response, it is noted that claim 29 of the instant application is directed to a reduced coenzyme Q10-containing composition comprising reduced coenzyme Q10, a polyglycerol fatty acid ester, and a fat and oil and/or a polyol, which is deemed generic to the claim 16 of the co-pending application 11/586,511 because said claim 16 recites the limitation of "polyglycerol fatty acid ester with a polymerization degree of glycerol being not lower than 3 and/or a condensed ricinoleic acid polyglyceride", and since vitamin E is disclosed as an art-recognized functional equivalent of vitamin C or its esters (see Chopra, rejection above), therefore, the two sets of claims are still deemed co-extensive in scope, and thus, the provisional ODP rejection of record is properly made. The use of various emulsifiers (such as polyglycerol fatty acid ester) and surfactants such as Tween and/or Span (alone and/or in combinations) to stabilize reduced coenzyme Q10 containing compositions would have been obvious to an artisan of ordinary skill

in the art based on the combined disclosures provided by Chopra and Motoyama et al (see rejection above), at the time the claimed invention was made.

In the absence of a terminal disclaimer, the ODP rejection is properly made and maintained.

Conclusion

NO claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SATYENDRA SINGH whose telephone number is (571)272-8790. The examiner can normally be reached on 9-5MF.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SUE X. LIU can be reached on 571-272-5539. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Satyendra K. Singh/
Examiner, Art Unit 1653

/Amber D. Steele/
Primary Examiner, Art Unit 1654